In re Application of: Yoram REITER et al.
Serial No.: 10/510,229
Filed: October 13, 2004
Office Action Mailing Date: June 18, 2008

Examiner: Zachariah LUCAS
Group Art Unit: 1648
Attorney Docket: 28429

REMARKS

Reconsideration of the above-identified application in view of the amendments above and the remarks following is respectfully requested.

Claims 141-160 and 197-212 are in this Application. Claims 150 and 200-211 have been withdrawn from consideration. Claims 141-149, 151-160, 197, 198 and 212 have been rejected under 35 U.S.C. §103. Claim 199 has been objected to. Claims 141 and 199 have been amended herewith. New claims 213 and 214 have been added herewith.

The Application now comprises, after amendments, claims 141-160, and 197-214, of which claims 141 and 199 are in independent form.

35 U.S.C. §103 Rejections

Reiter, Andersen and Chames

The Examiner has rejected claims 141-149, 151-155, 158, 159 and 212 under 35 U.S.C. §103(a) as being unpatentable over Reiter (1997, PNAS 94:4631-36), further in view of Andersen (WO Publication No. 97/02342) and Chames (2000, PNAS 97:7969-74). Specifically, the Examiner states that in the declarations by Professors Cerundolo and De Lisi it is nowhere specifies how the presentApplication overcomes the asserted deficiencies of the prior art. Further, the Examiner states that in view of the specific suggestions in the art that antibodies with the binding characteristics identified in the claims can be used for immunotherapeutic methods and as Chames specifically teaches the use of the same type of library and similar methodology to that disclosed in the present application for the identification of such antibodies, the assertions that the present application has met a previously unmet need is not found persuasive. Examiner's rejections are respectfully traversed. Claim 141 has been amended herewith. New claims 213 and 214 have been added herewith.

In contrast to Examiner's assertion that the methodology used by Chames is similar to that of the claimed invention, Applicants point out that while screening the antibody library according to either of Reiter (1997), Chames (2000) or Andersen (1997) is performed using liable complexes which are mixtures of three individual

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components, *i.e.*, the MHC heavy chain (e.g., HLA-A1 in Chames; mouse K^k in Andersen), β2-microglobulin and the antigenic peptide [See Chames et al., 2000, Pages 7970-7971 bridging paragraph; Andersen WO Publication No. 97/02342 Page 27, lines 1-5], screening the antibody library according to the instant Application is performed using a stable complex generated by refolding a single chain β2-microglobulin-Antigen presenting molecule (e.g., HLA-A2) with an antigen derived from a pathogen.

In fact the teachings of Chames et al., cannot be applied to the arts of Andersen and Reiter since the antibodies generated by Chames are low affinity binders which cannot bind cells in their soluble form and mediate cell killing, regardless of the target.

As is clearly evident from the screening results, using the teachings of the instant Application high affinity soluble antibodies (e.g., 25-30 nM; Page 75, lines 5-7 in the instant Application as filed) which are capable of specifically killing cells presenting the complex (Page 81, lines 2-11 in the instant Application as filed) were isolated from the same phage library used by Chames. Chames' screening method resulted in a single low affinity antibody (250 nM; Chames Page 7972, left column, lines 21-22) that failed in its soluble form to bind cells presenting the complex (See Chames Page 7972, left column, lines 23-26). In addition, in contrast to Examiner's assertion that Chames indicates that such a methodology would be useful for the identification of antibodies useful in immunotherapeutic methods, Applicants point out that Chames indicates that *"no other peptide-specific binders could be selected from the library... hence, such peptide-specific binders seem to be rare in the library despite its size"* (Chames Page 7973, right column, lines 22-26), thus Chames teaches away from using the same library to identify peptide-specific antibodies which can be efficiently used in a method of killing, as claimed. Thus, as was previously indicated in the declarations of Professors Cerundolo and De Lisi, the long felt need remained unresolved after Andersen, Reiter (who merely attached a toxin to Andersen's antibody) and Chames, either alone or in combination, since one of ordinary skills in the art would not have reasonable expectation of success and would not be motivated

to use the teachings of Andersen, Reiter and/or Chames for isolating T-cells like antibodies useful for therapeutic applications as claimed.

In order to render explicit what is already implicit, Applicants have amended claim 141 to limit the claimed invention to a "soluble" antibody, and have added new claims 213 and 214 pertaining to the use of complexes formed by a single chain human antigen-presenting molecule (produced in bacteria) being refolded with an antigen derived from a pathogen for screening the library.

Support for the amendment made in claim 141 ("soluble") can be found in Page 15, line 6 in the instant Application as filed.

Support for new claims 213 and 214 can be found in Page 65, lines 14-27 in the instant Application as filed.

Reiter, Andersen, Chames and Matsushita

The Examiner has rejected claims 141-149, 151-159 and 212 under 35 U.S.C. §103(a) as being unpatentable over Reiter (1997, PNAS 94:4631-36) in view of Andersen (WO Publication No. 97/02342) and Chames (2000, PNAS 97: 7969-74) as applied above, further in view of the teachings of Matsushita et al. (US Patent No. 5,591,829). Specifically, the Examiner states that Matsushita et al. teach antibodies targeting the pathogen antigen directly, instead of the MHC-antigen complex, however from the teachings of Reiter et al. regarding the virus infected cells, it would have been apparent to those of ordinary skill in the art that the antibodies of Reiter et al. and Andersen et al. would be functional equivalent for the antibodies of Matsushita et al. The Examiner's rejections are respectfully traversed.

Relying on the above arguments it is Applicants' position that the claimed invention cannot be rendered obvious by the teachings of Reiter et al., Andersen et al. and Chames et al., even when combined with the teachings of Matsushita et al., who merely teach antibodies directed against pathogenic epitopes. Withdrawal of the rejection is respectfully requested.

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Reiter, Andersen, Chames and Saito

The Examiner has rejected claims 141-149, 151-160 and 212 under 35 U.S.C. §103(a) as being unpatentable over Reiter (1997, PNAS 94:4631-36) in view of Andersen (WO Publication No. 97/02342) and Chames (2000, PNAS 97: 7969-74) as applied above, further in view of the teachings of Saito (2001, J. Virol. 75:1065-71). Specifically, the Examiner states that claim 160 requires that the antigen in the complex is a Tax protein polypeptide antigen and that Saito et al. teach that, in certain HTLV-1 infected patients, cells comprising HLA-A2/Tax peptide complexes appear to be involved in the pathogenesis of the disease, and that from these teachings, those of ordinary skill in the art would have been motivated to kill these cells in the indicated subgroup of HTLV-1 infected patients. The Examiner's statements are respectfully traversed.

Relying on the above arguments it is Applicants' position that the claimed invention cannot be rendered obvious by the teachings of Reiter et al., Andersen et al. and Chames et al., even when combined with the teachings of Saito et al., who merely teach the involvement of HLA-A2/Tax peptide complexes in certain HTLV-1 infected patients. Withdrawal of the rejection is respectfully requested.

Reiter, Andersen, Chames and Carter

The Examiner has rejected claims 141-149, 151-155, 158, 159, 197, 198 and 212 under 35 U.S.C. §103(a) as being unpatentable over Reiter (1997, PNAS 94:4631-36) and Andersen (WO Publication No. 97/02342) and Chames (2000, PNAS 97:7969-74) as applied above, further in view of Carter (US Patent No. 6,054,297). Specifically the Examiner states that claims 197 and 198 are directed to embodiments wherein the constant region of the antibody is capable of inducing antibody-dependent cell mediated toxicity or initiating a complement cascade and that Carter indicates that the use of such constant regions was known in the art, and therefore it would have been obvious to those of ordinary skill in the art to have used such constant domains in the immunotherapeutic antibodies suggested by the cited art. Examiner's rejections are respectfully traversed.

Relying on the above arguments it is Applicants' position that the claimed invention cannot be rendered obvious by the teachings of Reiter et al., Andersen et al. and Chames et al., even when combined with the teachings of Carter, who merely teach the use of constant domains in immunotherapeutic antibodies. Withdrawal of the rejection is respectfully requested.

In view of the above arguments, remarks and claim amendments, Applicants believe to overcome the 35 U.S.C. §103(a) rejections.

Double Patenting

Claims 141-149, 151-160, 197 and 198 have been provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4, 8, 11 and 13 of co-pending US Application No. 11/629,194, or the co-pending claims in view of the teachings of Reiter, Chames and Andersen and any of Matsushita, Saito or Carter as described above.

Applicants still respectfully request that the provisional rejections be held in abeyance until such time as claims are determined to be allowable or issue in the co-pending applications.

Claims Objected

The Examiner has objected to claim 199 as depending on a rejected claim.

Applicants have amended claim 199 to an independent form, to thereby overcome Examiner's objection.

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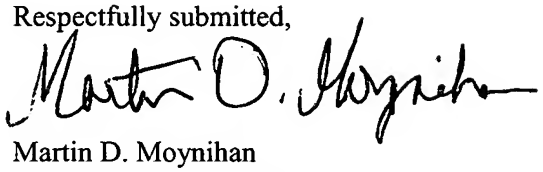
In view of the foregoing amendments and remarks, pending claims 141-149, 151-160, 197-199, and 212-214 are deemed to be allowable. A prompt Notice of Allowance is respectfully and earnestly solicited.

Respectfully submitted,



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Date: November 18, 2008

Enclosures:

- Additional Claims Transmittal Fee
- Petition for Extension of Time (Two Months)